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EXAMINER	
SCHWADRON, R	
ART UNIT	**PAPER NUMBER**
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DATE MAILED: 12/21/95

This is a communication from the examiner in charge of your application.
COMMISSIONER OF PATENTS AND TRADEMARKS

☒ This application has been examined ☐ Responsive to communication filed on _____ ☐ This action is made final.

A shortened statutory period for response to this action is set to expire 3 month(s), 0 days from the date of this letter. Failure to respond within the period for response will cause the application to become abandoned. 35 U.S.C. 133

Part I THE FOLLOWING ATTACHMENT(S) ARE PART OF THIS ACTION:

1. ☐ Notice of References Cited by Examiner, PTO-892.
2. ☒ Notice of Draftsman's Patent Drawing Review, PTO-948.
3. ☒ Notice of Art Cited by Applicant, PTO-1449.
4. ☐ Notice of Informal Patent Application, PTO-152.
5. ☐ Information on How to Effect Drawing Changes, PTO-1474.
6. ☐ _____.

Part II SUMMARY OF ACTION

1. ☒ Claims 1,2,4,5,19-24 are pending in the application.

   Of the above, claims _____ are withdrawn from consideration.

2. ☒ Claims 3,6-18 have been cancelled.

3. ☐ Claims _____ are allowed.

4. ☒ Claims 1,2,4,5,19-24 are rejected.

5. ☐ Claims _____ are objected to.

6. ☐ Claims _____ are subject to restriction or election requirement.

7. ☐ This application has been filed with informal drawings under 37 C.F.R. 1.85 which are acceptable for examination purposes.

8. ☐ Formal drawings are required in response to this Office action.

9. ☐ The corrected or substitute drawings have been received on _____. Under 37 C.F.R. 1.84 these drawings are ☐ acceptable; ☐ not acceptable (see explanation or Notice of Draftsman's Patent Drawing Review, PTO-948).

10. ☐ The proposed additional or substitute sheet(s) of drawings, filed on _____. has (have) been ☐ approved by the examiner; ☐ disapproved by the examiner (see explanation).

11. ☐ The proposed drawing correction, filed _____, has been ☐ approved; ☐ disapproved (see explanation).

12. ☐ Acknowledgement is made of the claim for priority under 35 U.S.C. 119. The certified copy has ☐ been received ☐ not been received ☐ been filed in parent application, serial no. _____ ; filed on _____.

13. ☐ Since this application apppears to be in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under Ex parte Quayle, 1935 C.D. 11; 453 O.G. 213.

14. ☐ Other

EXAMINER'S ACTION

15. Claims 1,2,4,5,19-24 are under consideration.

16. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman,* 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321 (b) and (c) may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

17. Claims 1,4,5,19-24 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 6-9 of copending application Serial No. 08/478967. Although the conflicting claims are not identical, they are not patentably distinct from each other for the following reasons. Claim 20 is included as reading on claim 18, not 8, because the antibody of claim 20 is not recited in the method of claim 8. While claims 6-9 differ in scope from claims 1,4,5,21-24 in that claims 6-9 encompass certain specific combinations of antibodies not recited in claims 1,4,5,21-24, both sets of claims

encompass the treatment of B cell lymphoma using antibody derived from transfectoma ATCC 69119. While claims 6-9 differ in scope from claims 19 and 20 in that claims 6-9 encompass certain specific combinations of antibodies not recited in claims 19 and 20, both sets of claims encompass the treatment of B cell lymphoma using antibody derived from transfectoma ATCC 69119 and HB 11388. The dosages and time schedule for administration of the aforementioned antibodies are overlapping in the two sets of claims. Therefore, the two sets of claims under consideration in this rejection would have been prima facie obvious in view of each other to one of ordinary skill in the art at the time the invention was made for the aforementioned reasons.
This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

18. Claims 19 and 20 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claim 18 of copending application Serial No. 08/475,813. Although the conflicting claims are not identical, they are not patentably distinct from each other because of the following reasons. Claims 19 and 20 differ in scope from claim 18 in that claim 18 specifies a specific species for each antibody in the claim, while claims 19 and 20 only specify a species for one of the antibodies recited in the claim. However, both sets of claims read on the use of chimeric antiCD20 antibody followed by the use of radiolabelled antiCD20 antibody. Therefore, the two sets of claims under consideration in this rejection would have been prima facie obvious in view of each other to one of ordinary skill in the art at the time the invention was made for the aforementioned reasons.

This is a *provisional* obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

19. Drawings have been submitted which fail to comply with 37 CFR 1.84. Please see the enclosed form PTO-948.

20. The use of the trademarks MILLI-Q AND ALCONOX has been noted in this application. It should be capitalized wherever it appears and be accompanied by the generic terminology.

Although the use of trademarks is permissible in patent applications, the proprietary nature of the marks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

21. Applicants need to update the status of the US patent applications (eg. abandoned, etc.) disclosed in the specification. Applicant needs to change 09/147,696 to 08/147,696 because this is the correct serial number for the application listed on page 1 of the specification, line 27.

22. Applicants need to list the appropriate sequence ID number after the sequence disclosed on page 22, line 21 of the specification.

23. The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

The specification is objected to under 35 U.S.C. § 112, first paragraph, as failing to adequately teach how to make and/or use the invention, i.e. failing to provide an enabling disclosure and failing to present the best mode contemplated by the applicant for carrying out the invention.

A) It is apparent that the chimeric antiCD20 antibody derived from the transfectoma known as ATCC 69119 is required to practice the instant invention as cited in claims 1,2,4,5,19,21-24 which recites this antibody. As a required element, the transfectoma producing the aforementioned antibody must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If said antibody is not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the instant hybridoma. See 37 CFR 1.802.

The specification does not provide a repeatable method for obtaining the antibody produced by the transfectoma ATCC 69119. While the sequences of said antibody are disclosed in the specification, there is no indication that the antibodies produced by the deposited transfectoma would have the identical sequence (eg. due to somatic mutation). Furthermore, antibodies based on the sequences disclosed in the specification would not necessarily have the same glycosylation pattern as that seen by antibodies produced by the claimed transfectoma and sites of glycosylation are not disclosed in the sequence. Finally, the claims read on antibody produced by a specific deposited transfectoma. Deposit of the transfectoma producing the aforementioned antibody would satisfy the enablement requirements of 35 U.S.C. 112.

In addition, the identifying information set forth in 37 CFR 1.809 (d) should be added to the specification. See 37 CFR 1.801-1.809 for additional explanation of these requirements.

While the aforementioned transfectoma has been deposited with the ATCC under conditions of the Budapest Treaty, applicants need to supply the date that ATCC 69119 was deposited with the ATCC, and meet the requirements under 37 CFR 1.808. The requirements under 37 CFR 1.808 can be met by submission of an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has

been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability of the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808. Claims 1,2,4,5,19,21-24 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

B) It is apparent that the monoclonal antibody produced by hybridoma known as ATCC HB11388 is required to practice the instant invention as cited in claim 20 which recites this antibody. As a required element, the hybridoma producing the aforementioned antibody must be known and readily available to the public or obtainable by a repeatable method set forth in the specification. If said antibody is not so obtainable or available, the enablement requirements of 35 U.S.C. 112, first paragraph, may be satisfied by a deposit of the instant hybridoma. See 37 CFR 1.802..

The specification does not provide a repeatable method for obtaining the hybridoma ATCC HB11388. While the sequences of said antibodies are disclosed in the specification, there is no indication that the antibody produced by the deposited hybridoma would have the identical sequence (eg. due to somatic mutation). Furthermore, antibodies based on the sequences disclosed in the specification would not necessarily have the same glycosylation pattern as that seen by antibodies produced by the claimed hybridoma and sites of glycosylation are not disclosed in the sequence. Finally, the claims read on antibodies produced by a specific deposited hybridoma. Deposit of the hybridoma producing the aforementioned antibody would satisfy the enablement requirements of 35 U.S.C. 112.

In addition, the identifying information set forth in 37 CFR 1.809 (d) should be added to the specification. See 37 CFR 1.801-1.809 for additional explanation of these requirements.

While the aforementioned hybridoma has been deposited with the

ATCC under conditions of the Budapest Treaty, applicants need to meet the requirements under 37 CFR 1.808. The requirements under 37 CFR 1.808 can be met by submission of an affidavit or declaration by applicants or someone associated with the patent owner who is in a position to make such assurances, or a statement by an attorney of record over his or her signature, stating that the deposit has been made under the terms of the Budapest Treaty and that all restrictions imposed by the depositor on the availability of the public of the deposited material will be irrevocably removed upon the granting of a patent, would satisfy the deposit requirements. See 37 CFR 1.808. Claim 20 is rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

24. Claims 1,2,4,5,19-24 are rejected under 35 U.S.C. § 112, first paragraph, for the reasons set forth in the objection to the specification.

25. The following is a quotation of 35 U.S.C. § 103 which forms the basis for all obviousness rejections set forth in this Office action:

> A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.
>
> Subject matter developed by another person, which qualifies as prior art only under subsection (f) or (g) of section 102 of this title, shall not preclude patentability under this section where the subject matter and the claimed invention were, at the time the invention was made, owned by the same person or subject to an obligation of assignment to the same person.

26. Claims 19 and 20 are rejected under 35 U.S.C. § 103 as being unpatentable over Grossbard in view of Anderson et al.

Regarding priority for the instant application with regards to prior art, the claimed invention is not disclosed in parent application 07/978891 and therefore priority for the instant application for the purpose of applying prior art is parent application 08/149099. Claim 20 is included as reading on claim 18, not 8, because the antibody of claim 20 is not recited in the method of claim 8. The claims are drawn to a method of treating B cell lymphoma with the antibodies recited in the claims. Grossbard et al. teach that unconjugated murine antiCD20 antibody was used for the treatment of B cell lymphoma (see Table 2).Grossbard et al. teach that radiolabelled antiCD20 antibody was used for the treatment of B cell lymphoma (see Table 6). Grossbard et al. teach the use of unlabelled antibody, followed by radiolabelled antibody for the treatment of human lymphomas (see page 874, second column, last paragraph). In view of the fact that murine antiCD20 had been used for the treatment of B cell lymphoma, it would have been obvious to a routineer that a chimeric antiCD20 antibody could have been used for treating B cell lymphomas based on the art known advantages of chimeric over murine antibodies. A routineer would have used a chimeric antibody in combination with a radiolabelled murine antibody because Grossbard et al. teach that radiolabelled chimeric antibodies would be therapeutically inferior to radiolabelled murine antibodies because "prolonged serum half-life of humanized RAbs may result in a substantial increase in nonspecific total body irradiation."(page 873, first column, last paragraph). Grossbard et al. do not teach the use of the specific antibodies recited in the claim.

Anderson et al. teach a chimeric anti-CD20 antibody which has the variable region of murine antibody 2B8 attached to a human G1 K construct (see third sentence of Abstract). This antibody is called c2B8 (see Abstract, line 7). This antibody appears to be the same as that disclosed in the specification in that both antibodies

consist of the V region of 2B8 (see specification, page 40-42) attached to a human G1 K construct (see specification, page 21), and both antibodies are called c2B8 (see specification page 40, line 10). Anderson et al. teach that said antibody is produced by a vector expressed in mammalian cells (eg. a transfectoma). Anderson et al. teach the 2B8 murine antibody, which is the antibody produced by the hybridoma recited in the claim(see specification, page 62). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have combined the teachings of the cited references to produce the method of the instant invention because Grossbard teaches the use of unlabelled antibody, followed by radiolabelled antibody for the treatment of human lymphomas and Grossbard et al. teach that radiolabelled chimeric antibodies would be therapeutically inferior to radiolabelled murine antibodies because "prolonged serum half-life of humanized RAbs may result in a substantial increase in nonspecific total body irradiation."(page 873, first column, last paragraph).

27. Claims 1,2,4,5,21-24 are rejected under 35 U.S.C. § 103 as being unpatentable over Robinson et al. (WO 88/04936) in view of Anderson et al.

The claims are drawn to a method of treating B cell lymphoma with the chimeric antiCD20 antibody ATCC 69119. Robinson et al. teach that chimeric antiCD20 antibodies can be used for therapeutic purposes (see page 29). Robinson et al. do not teach the use of antibody ATCC 69119 for the treatment of B cell lymphoma. Anderson et al. teach a chimeric anti-CD20 antibody (see Abstract). The antibody taught by Anderson et al. is immunologically active (eg. it can mediate human complement mediated lysis, see Abstract). This antibody is called c2B8 (see Abstract, line 7). This antibody appears to be the same as that disclosed in the specification in that both antibodies consist of the V region of 2B8 (see specification, page 40-42), both antibodies are of the same isotype

(G1/ K) and both antibodies are called c2B8 (see specification page 40, line 10). Anderson et al. teach that said antibody is produced by a vector expressed in mammalian cells (eg. a transfectoma). Anderson et al. teach that said antibody has the "ability to target B cell lymphomas" (see abstract). It would have been prima facie obvious to one of ordinary skill in the art at the time the invention was made to have created the instant invention because Robinson et al. teach that chimeric antiCD20 antibodies can be used for therapeutic purposes and Anderson et al. teach that the antiCD20 antibody known as ATCC 69119 has the "ability to target B cell lymphomas". A routineer would have determined the claimed particular schedule of administration and dosage of antibody for use in the claimed method using routine experimentation.

28. No claim is allowed.

29. Papers related to this application may be submitted to Group 180 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Papers should be faxed to Group 180 at (703) 305-7401.

30. Any inquiry concerning this communication or earlier communications from the Examiner should be directed to Dr. Ron Schwadron whose telephone number is (703) 308-4680. The examiner can normally be reached Tuesday through Friday from 8:30 to 6:00. The examiner can also be reached on alternative Mondays. A message may be left on the examiners voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Ms Margaret Moskowitz Parr can be reached on (703) 308-2454. Any inquiry of a general nature or relating to the status of this application should be directed to the Group 180 receptionist whose telephone number is (703) 308-0196.

RONALD B. SCHWADRON
PATENT EXAMINER
GROUP 1800

Ron Schwadron, Ph.D.
Patent Examiner
Art Unit 1816
December 19, 1995